MEDICAL PROCEEDINGS

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Although South Africa is so far away from the world's main scientific centres, the therapeutic introduction of radio-active isotopes was not long delayed and occurred before radon, although the latter had been used for many years in the United States and Europe. Failla[1] had, indeed, introduced the gold filtration of radon in the United States in 1926.

Radon had, of course, been used before 1926, but until then it had been in glass capsules, the beta radiation causing a great deal of necrosis in the surrounding tissue.

Radon was first used in South Africa in 1950, i.e. about 25 years after the introduction of the gold filtration and over 40 years since radon was first used in glass capsules, whereas the radio-active isotopes were introduced into South Africa in 1948, 10 years after isotopes therapy was started by Hamilton and Stein[2] in the U.S.A. South Africa was thus using radio-active isotopes for medical purposes as early as Great Britain and continental Europe.

The difficulty about radon in South Africa was its short half-life and it was not until the fast air service was started that the importation of radon became possible. Only after discussions with the authorities at Amersham during visits to Great Britain in 1949 and 1950 were satisfactory arrangements made for radon importation.

The early introduction of radio-active isotopes for medical purposes into South Africa was partly due to the fact that a good deal of local interest had been aroused in 1945 about the possibility of treating giant follicular lymphoma, Hodgkin's disease and the blood dyscrasias with radio-active phosphorus. As it was not possible to import radio-active phosphorus in 1945 because of the ban on export of the isotopes from the U.S.A., a visit to the United States to study this aspect was arranged with the kind help of General A. J. Orenstein, Director General of Medical Services for the Army, at the request of Col. M. M. Suzman.

The visit stimulated an interest in the isotopes, but it was impossible to arrange to import them into this country at that time.

In 1947 one of us (M. W.) attended the International Cancer Congress in St. Louis, U.S.A., as the representative of the National Cancer Association of South Africa. A message from President Truman to this Congress stated that the export of radio-active isotopes from the U.S.A. would in future be permitted, on certain conditions. The conditions laid down by the

*Based on a lecture-demonstration in Pretoria in July 1957 at the *Conference on Isotopes* of the Scientific Council for Africa South of the Sahara.

United States were transmitted to the national representatives. These were forwarded to the C.S.I.R. by the National Cancer Association of South Africa in October 1947 and the C.S.I.R. took immediate steps to obtain isotopes.

By 1948 we were, therefore, able to use radio-active phosphorus in therapeutic doses and radio-active iodine in tracer doses.[3]

The introduction of the isotopes was not without difficulties. The gamma-emitting isotopes could only be obtained in tracer quantities because of the amount of protection required by the regulations for their transport by air. We could, therefore, start with tracer doses of radio-active iodine only. We could, however, get radio-active phosphorus. Air travel at that time was not as fast as to-day, and one had to allow for a considerable amount of decay before the isotopes reached us. Moreover, Johannesburg was the air terminal and because it meant a change of planes to get the isotopes to other centres, e.g. Cape Town, the use of the isotopes was confined to Johannesburg and Pretoria until Great Britain began to produce radio-active isotopes. The use of isotopes away from Pretoria and Johannesburg has, however, been limited both by the difficultis of transport and by the stringent regulations laid down by the C.S.I.R., and more recently by the Atomic Energy Board.

In the earlier years there were few radiotherapists and medical men interested in the subject, but in recent years there has been a keener demand for isotopes for medical purposes. The regulations (very similar to those abroad) make it impossible for those who have not had an opportunity to study the isotopes or who have not got the facilities which the Atomic Energy Board expects (in the form of protection and skilled physical supervision) to use these isotopes.

In the first place, those who wish to use isotopes must show that they have had experience and training in the subject, even though they may have held qualifications in radiotherapy for many years; secondly, they must show that they are equipped to ensure the safety of personnel.

The greatest stumbling block, as far as the regulations are concerned, is the difficulty of obtaining hospital physicists, on which the Atomic Energy Board insists. The definition of a hospital physicist is a physicist who, apart from holding a qualification such as the M.Sc., has had a minimum amount of training of a year or two, in the case of a B.Sc. (Honours), in a hospital radiotherapy department, where radiotherapy with isotopes is practised apart from X-radiation and gamma radiation. The hospital physicist literally did not exist in that sense in South Africa until recently, and it was quite impossible, particularly for those in private or hospital practice, to obtain the services of a suitable physicist. While there is a Hospital-Physicist Society in Great Britain (with about 150 members) they are all in employment and even tempting offers failed to induce any of them to come to South Africa. This deficiency is being made good now by a number of South Africans being sent overseas to be trained. Large centres, e.g. Cape Town, do not use isotopes at the Groote Schuur Hospital because their full-time hospital physicist left for an overseas appointment and the present physicist did not have the requisite hospital training. (He is overseas now for that purpose.) In other large centres, e.g. East London, Port Elizabeth and Durban, no isotopes are being used at present. In Durban the Radiotherapy Department is being rebuilt and reorganized at the Addington Hospital and the isotopes should be used there within a few months.[44]

In Johannesburg a considerable quantity of the various isotopes applicable to diagnosis and therapy, is being used both at the General Hospital and in private practice. In Pretoria a lesser quantity is used at the hospital and very little in private practice. In Pretoria, too, a new Radiotherapy Department is being built at the hospital. On its completion much greater use of the isotopes will be made both for research and therapy.

The isotopes used vary little from those employed abroad, as far as diagnosis and therapy are concerned. The only limitations are the very short half-life isotopes which are difficult to import because of the distance from London and the massive quantities used for telecurie therapy.

The large quantities of cobalt^{60} or caesium^{137} necessary for teletherapy are not yet available in South Africa and will not be available from Great Britain for another 2–3 years. A recent letter from Harwell to the National Cancer Association stated that cobalt would be available at the end of 1958 and caesium in 1960. There is no doubt that the larger hospitals will obtain cobalt and caesium bombs when these and the personnel with the requisite skill become available. The short half-life isotopes, such as sodium^{24} and bromine^{82} are of little importance in practical therapeutics and can be substituted by others. With the increasing speed of aeroplanes and the fact that a cyclotron has been built in Pretoria, the radiotherapists will be able to use even these if there is

any particular virtue in any short-life isotope. It must be recalled that the cyclotron is an expensive instrument and the isotopes it produces are much more expensive than the corresponding isotopes produced in an atomic pile. About 2 years ago our Chairman (Professor Naude) pointed out that an atomic pile for power purposes in South Africa is some time off because of the abundance of fuel; and even if an atomic pile were built it would be probably situated in the Cape rather than in Johannesburg, which has the coal fields at its front door, as it were, and oil at its back door.

On the scientific side, as long ago as 1942, Lawrence[4] stated that enough work had already been done to indicate that the radio-active isotopes will rival the microscope in scientific usefulness. Hahn and Sheppard[5] and Byron Hall[6] were already of the opinion in 1947 that radio-active isotopes would ultimately surpass the value of X-rays and radium together as a therapeutic agent. Now, 10 years later, there is little doubt that this will prove to be the case when the large caesium plants come into operation in Great Britain in 1960 and cobalt becomes more readily available. It is not within the scope of this paper to compare caesium and cobalt with the standard X-ray machines, but it is obvious that although a use for the standard X-ray machine up to the 250 K.V. range will always be found, according to a recent symposium on the subject[7] the caesium and cobalt bombs will be in general use when personnel and these isotopes became available.

Tables 1 to 3 indicate the therapeutic isotopes which are generally used abroad. Within the limitation I have already mentioned, i.e. the short half-life isotopes (e.g. sodium) and the large quantities used for telecurie purposes, we have also used these isotopes for diagnostic and therapeutic purposes. We use P^{32} but not Na^{24}, because of its short half-life. We do not use iodine[130] and I do not know of anybody who uses it now for medical purposes, although it will be recalled that it was used in the early work in the diagnosis and treatment of thyrotoxicosis. Iodine[131] is used in considerable quantities and is probably the most important of the isotopes used in South Africa. It will be seen from Dr. E. J. Marais' paper[43] that most money was spent in this country on the importation of this isotope during 1956–57. It was used entirely in Johannesburg and Pretoria. Iodine[131] is used for the diagnosis and treatment of hyperthyroidism as well as for carcinoma of the thyroid. Its use in hyperthyroidism is not mentioned in the last column of Table 1 because the Table refers to a paper on the radio-isotopes in cancer therapy.[8]

We have not used manganese or silver but we use cobalt in a variety of ways for surface applicators and intra-cavitary techniques. We have not got the large quantities necessary for telecurie therapy purposes.

TABLE 1: THERAPEUTIC TECHNIQUES

External Methods	
1. Telecurie: Co^{60}, Ir^{192}, Caesium[137].	
2. Plaque: Co^{60}, P^{32}, Ruthenium[106].	
3. Contact surface and strontium eye applicators: Colloidal Gold, P^{32}.	
4. Interstitial needles: Co^{60}, Yttrium, Tantalum.	
5. Direct infiltration: Au^{198}, Ag^{111}, Colloidal Chromium Phosphate, P^{32}.	
6. Intra-cavitary: Co^{60}, Na^{24}, Au^{198}.	
7. Intra-peritoneal and intrapleural: Au^{198}, Colloida Chromium Phosphate.	
8. Retention enema: Au^{198}, Ag^{111}.	These have been suggested
9. Gastrointestinal by Miller-Abbott tube: Au^{198}.	
10. Intra-pulmonary (direct inhalation): Krypton or Aerosol.	
11. *In Vivo* Fission: Colloidal uranium oxide, by neutron bombardment.	

TABLE 2: ORAL AND INTRAVENOUS

1. P^{32}	14·3 days	Blood dyscrasia and colloid for the reticulo-endothelial system.
2. Na^{24}	14 hours	General internal radiation.
3. I^{131}	8 days	Selective localization. Thyroid.
4. Au^{198} Colloidal Chromium Phosphate		Intravenous for the reticulo-endothelial system and secondary pulmonary deposits. Liver, spleen, lymphomas.

Iridium[192] is unavailable here. Several years ago, after a visit to Professor Mitchell at Cambridge, I attempted to get an iridium bomb of the type he uses, but because of the short half-life of iridium (only 70 days) and the difficulties of transportation by air more than a small quantity at a time, it did not prove possible to get sufficient for a bomb.

We use strontium[90] in the form of eye applicators, but do not use the various strontium isotopes the Table mentions for therapy in bone tumours. Tantalum[82] has been used at the Johannesburg General Hospital. We have used yttrium[90] in several cases of secondary deposits from carcinoma of the breast, for im-

TABLE 3

Isotope	*Half-Life*	*Radiation*	
P^{32}	14·3 days	β	Blood dyscrasias. Local treatment.
Na^{24}	14·8 hours	β and γ	Local and bladder. General body radiation.
I^{131}	8·0 days	β and γ	Secondary deposits.
Au^{198}	2·7 days	β and γ	Intraperitoneal and pleural and direct infiltration and implantation.
Mn^{52}	6·5 days	β and γ	In colloid form for the reticulo-endothelial system.
Ag^{111}	7·5 days	β	Local infiltration.
Co^{60}	5·3 years	β and γ	Teletherapy plaque and interstitial. 13·5 r/hr./mc. at 1 cm. Rad. r/hr./mc. at 1 cm. (8·3 r).
Ir^{192}	70 days	β and γ	Teletherapy.
Sr^{85}	55 days	β	Eye and surface applicators.
Tal^{82}	111 days	β and γ	Interstitial and eye applicators.
Y^{90}	65 hours	β	Interstitial. Pituitary implants.

plantation into the pituitary fossa. We had been using radon until yttrium was introduced.[9]

THERAPEUTIC ISOTOPES IN SOUTH AFRICA

A. DIAGNOSTIC PURPOSES

1. *By Auto-Radiography.* A biopsy specimen removed after administration of the isotope on the previous day may be put on photographic emulsions. The extent to which these are affected indicates to what extent tissues take up the isotope and where these tissues are located.[10] This is a very valuable method for determining the radio-active iodine uptake and localization in the treatment of cancer of the thyroid (Figs. 1, 2).

A variation of this method, which can be used *in vivo,* is to place X-ray films over the parts suspected to see whether any radiation is emitted. The first secondary deposit from a carcinoma of the thyroid was demonstrated in this way by Keston[11] in 1942 in a femur.

2. *Detection of gamma or beta rays* given off by any particular tissue after administration of the appropriate isotope, e.g. P^{32} for brain tumours, iodine^{131} for the external demonstration of brain tumours and thyroid carcinoma and in thyrotoxicosis with Geiger and scintillation counters.

Apart from radio-active iodine, with which I shall deal presently, and apart from the use of phosphorus in the demonstration of the extent of brain tumours, the isotopes have not played any great part in the diagnosis of malignant disease.

Radio-active iodine in the form of di-iodofluorescein, later given simply as radio-active iodine, was used for the demonstration of brain tumours by external counting by Moore.[12] American workers claimed a considerable degree of accuracy, but their results could not be duplicated in Great Britain at the Cancer Hospital (Smithers) nor could we get any definite result in a number of cases here.

Much greater success has, however, been obtained with radio-active phosphorus in the demonstration both of the extent of a brain tumour before operation and the extent of its removal after operation.[13] It has also proved of particular value in demonstrating the site

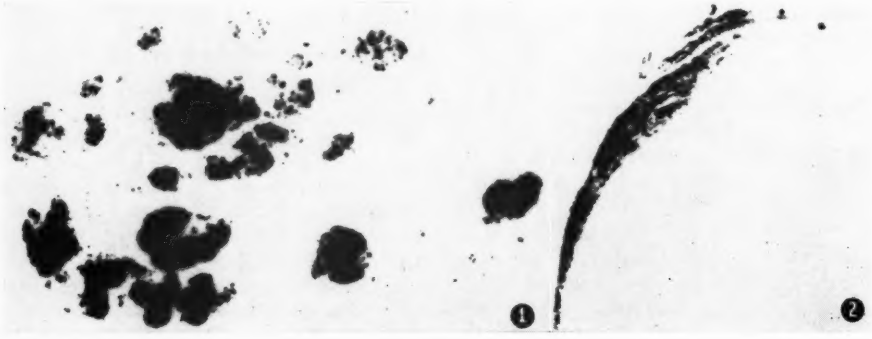


Fig. 1. Autoradiograph of a case of thyroiditis diagnosed clinically as a carcinoma. Note the irregular uptake of the radio-active iodine.

Fig. 2. Autoradiograph of a carcinoma of the thyroid. Note there is no uptake except at the margins and this uptake is probably in normal thyroid.

from which the biopsy material should be taken.

This method of investigation involves the use of the Selverstone probe through a burr hole in the skull after an intravenous dose of half-a-millicurie of phosphorus some 24 hours before the investigation. A 2 mm. Selverstone probe was introduced in the U.S.A. This probe contains a miniature Geiger counter at the end of the metal container which is only 2 mm. in diameter and some 4 inches long. This probe is very fragile and expensive. A 3 mm. probe 6 inches long has been introduced in Great Britain both for the demonstration of mobility of the head of the fractured femur (thus giving an indication whether union is likely to take place or whether surgical intervention should be carried out immediately) and for the demonstration of brain tumours in the same manner as with the 2 mm. probe.[14]

We have not used the probes for the demonstration of the condition of femoral heads, but we have done a number of brain cases with Mr. E. M. Kerr and Mr. H. Mendelow, with very satisfactory results.

The basis for this method of diagnosis is the fact that brain tumours will pick up more radio-active phosphorus than will the surrounding brain tissue. Normally the grey matter takes up more than the white matter, so that as the probe is inserted high counts are obtained through the first 2 cm. as the probe passes through the grey matter. The counts then become very low until the tumour is penetrated, when there is a sharp rise in the count. The point at which most counts are obtained is obviously the site at which the biopsy should be taken. In this way specimens giving a positive diagnosis have been obtained where previous attempts through the same burr hole had failed.

Fig. 3 depicts the counts as the probe penetrates the brain in various directions, this outlining the tumour and also indicating the best position for biopsy. The probe is very sensitive and even minute quantities of tumour tissue will register higher counts than will the surrounding tissue.

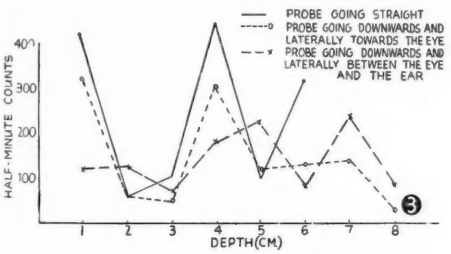
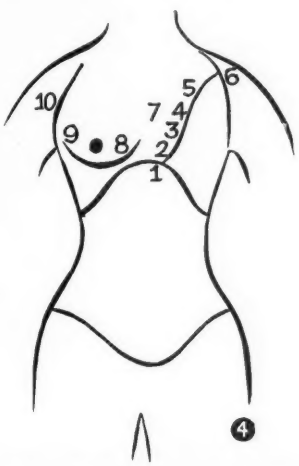


Fig. 3. Uptake of P^{32} in a brain tumour with the Selverstone probe.
This probe was inserted at various angles to determine the extent of the tumour.

The late Professor Low-Beer[15] used radio-active phosphorus to diagnose or establish the differential diagnosis between skin nodules due to secondary deposits from carcinoma of the breast and other conditions. As the beta particle only has a maximum penetrating power of about 8 mm. in tissue, it can only be used for superficial conditions (Fig. 4). Professor Low-Beer tried, with P^{32} to differentiate between multiple myelomata and secondary deposits from breast carcinoma, but with poor results. In any case, an expert radiologist should have little difficulty in establishing the differential diagnosis between these conditions. P^{32} has been suggested for the differential diagnosis in ocular melanomata.[16]

Apart from the demonstration of brain tumours, P^{32} has not proved of great value in diagnostic procedures. One difficulty is that inflammatory tissue will take up more radio-active phosphorus than will the surrounding tissue, and it therefore becomes difficult to be certain whether one is dealing with secondary deposits or an inflammatory condition.

We have, however, found radio-active iodine of great value in demonstrating secondary deposits from those cancers of the thyroid which take up the radio-active iodine. Figs. 5A, 5B, 5C show a large secondary deposit in a skull very clearly demarcated by radio-active iodine.



1. 1,502
2. 2,001
3. 2,034
4. 1,876
5. 2,070
6. 1,800
7. 1,445
8. 1,363
9. 1,226
10. 1,838

Fig. 4. P^{32} uptake in nodules in the scar of a mastectomy for a carcinoma.

It is true it shows up in the X-ray films, but the disease extends beyond the margins of the lesion shown in the films. The films can only show the actual tissues which have been destroyed or altered. Similarly, in the case illustrated in Figs. 6A, 6B, 6C, the radio-active iodine showed up secondary deposits in the pelvis, various lumbar and dorsal vertebrae and it proved a blessing to this woman who had been bedridden and was in great agony. She could not be moved for X-ray treatment and we consequently treated her with radio-active iodine. Although some hundreds of millicuries had to be used over a period of 2 years, she made an excellent recovery and is now able to walk about free from pain.

Radio-active iodine is also used in the negative sense to show whether nodules in the thyroid are inactive or not. If in the nodular thyroid which takes up radio-active iodine a

Fig. 5A. A large secondary deposit in the skull from the thyroid.

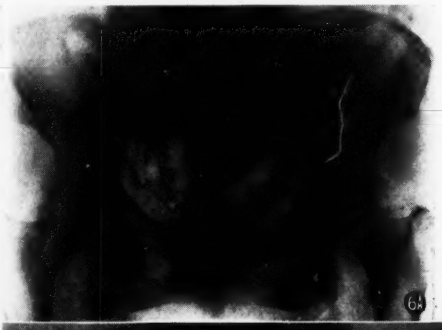
Fig. 5B. A marker has been placed around a defect in the skull and iso-counts outlined with a Veal gun. These indicate that the bone is involved for a considerable distance beyond the margin.

Fig. 5C. The patient complained of pain in the region of the left sacro-iliac joint. The X-ray films do not reveal any secondary deposits but the differential counts show a high radio-active iodine uptake.

nodule is found which does not take up any of the iodine, there are very strong grounds for suspecting that the nodule is malignant. The 'gun' designed by Veal[17] and a similar apparatus described by Dobyns and others in 1949 is used to get differential counts over small areas. The apparatus consists of a small Geiger tube heavily shielded. It is held by a handle which gives it the appearance of a gun.

Apart from its value in the demonstration of malignant portions of the thyroid or secondary deposits from the thyroid, radio-active iodine has proved of the greatest value in the diagnosis of thyrotoxicosis. The thyroid takes up 10,000 times more radio-active iodine than does any other tissue.[18] The thyroid of the thyrotoxic patient has been stated to be 5–6 times more sensitive than the normal thyroid. It follows, therefore, that if a tracer dose of radio-active iodine is given, the thyroid takes up the radio-active iodine almost completely to the exclusion of the other tissues. The isotope is excreted through the urine. The uptake of the radio-active iodine by the thyroid starts within the first few minutes and continues until it reaches a maximum, in most cases at 24 hours.

If the normal range and the upper normal limit are established, then the means of diagnosing thyrotoxicosis is provided. Numerous tests have been devised for the diagnosis of thyrotoxicosis with radio-active iodine tracers. To get a quick result, it has been suggested that the 1-hour uptake should be measured.[19] Others favour the 2-hour, 4-hour, 8-hour intervals.[20] There is no reason why several tests should not be made at varying intervals and, in fact, they should be made so that there is a check on the tests. If the uptake at 1 hour is within normal limits or is low, the uptake



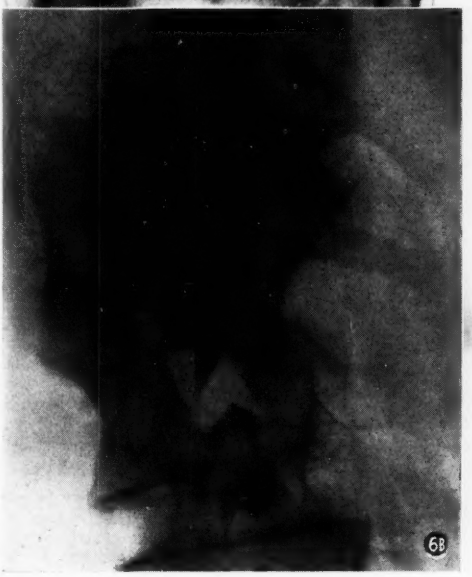


Fig. 6A. Destruction of the left side of the sacrum by a secondary deposit from the thyroid.

Figs. 6B, 6C. Destruction of the first lumbar vertebra by a secondary deposit from the skull with marked angulation.

Both patients did remarkably well on radio-active iodine treatment.

at the other intervals is not likely to be higher than the normal for that period. As the radio-active iodine is excreted in the urine, there is obviously a further means of checking on the tests by measuring the urinary amount excreted at various intervals. It has been found[21, 22] that although the amount excreted between 0 and 8 hours is very much the same for the hyperthyroid and the euthyroid patient there is a distinct difference in the amount excreted between 8 and 24 hours. During this interval the hyperthyroid patient excretes much less than does the euthyroid patient.

There is still another test, the Conversion Ratio,[23, 24] i.e. the amount of radio-active protein-bound-iodine compared with the total radio-active iodine in the serum. Although this test is rather laborious, it is of great value as an index of the amount of radio-active iodine which is converted into hormone. It does not always follow that a high uptake of radio-active iodine also means that a great deal of hormone is formed. In some types of cretins, e.g. the radio-active iodine uptake is high but the amount converted into hormone is low.[25]

Very few tests in clinical medicine ever show a razor-sharp line of demarcation between the normal and abnormal. This is particularly true with the B.M.R. test for thyrotoxicosis. It also applies to the protein-bound-iodine test, although this is considerably more accurate than is the B.M.R. test. With the radio-active iodine test there is also some overlap in the uptakes between the hyperthyroid and the normal and the normal and the hypothyroid. The overlap between the hyperthyroid and the euthyroid is, however, not very great. The upper normal limit given by various observers described in the literature, and as we have found it in hundreds of cases, is strikingly similar. We take our upper normal figure as 15% uptake at 1 hour, 40% at 5 hours and 50% at 24 hours. Our upper normal for the Conversion Ratio is 40% at 24 hours.[26]

The graphs we have obtained in analysing a number of normal thyroid cases for uptake, excretion and for the Conversion Ratio were

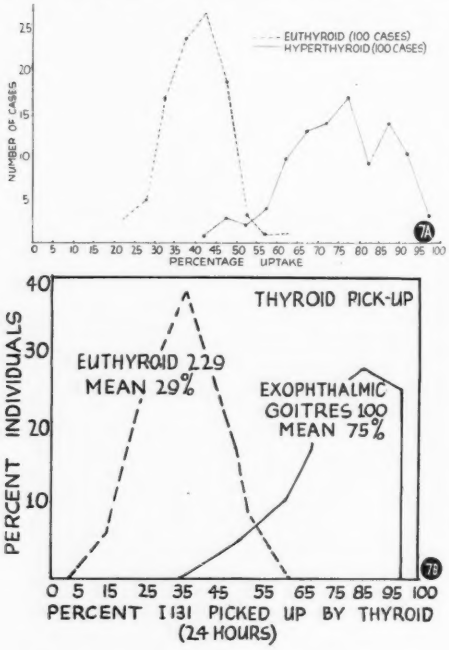


Fig. 7A. 24-hour uptake in 100 euthyroid and hyperthyroid cases.

Fig. 7B. Values obtained by Seed, Jaffe and Baumeister. Note the similarity of the curves and that in our cases and Seed's case the curves cross at 55%.

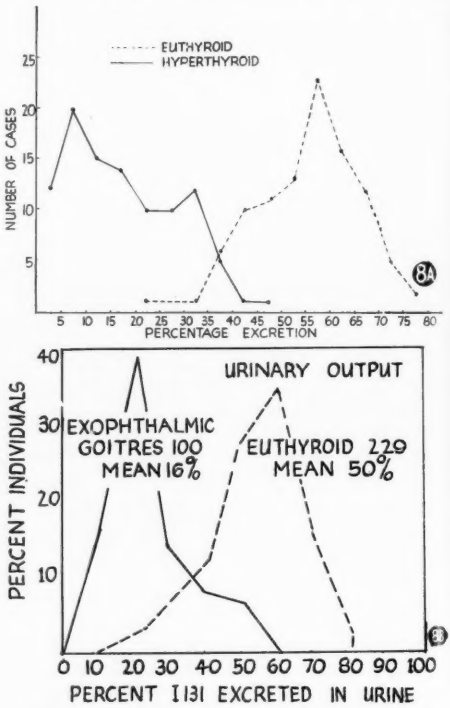


Fig. 8A. 24-hour excretion in 100 euthyroid and hyperthyroid cases.

Fig. 8B. Seed's values. Note again the similarity of the curves.

strikingly similar to those published in the literature.[26] Figs. 7A, 7B, 8A and 8B show this similarity.

We have investigated some 700–800 patients with radio-active iodine tracer tests. Some of the patients, of whom 350 have been treated for thyrotoxicosis, have been investigated a number of times and we have found the radio-active iodine uptake test (if more than one test is done with the same tracer dose, i.e. the uptake not only at 24 hours but at some intervening period as well as estimating of the Conversion Ratio) is more accurate than the B.M.R. or the P.B.I. (protein-bound-iodine) tests. This has been confirmed by a number of reports in the literature.[27]

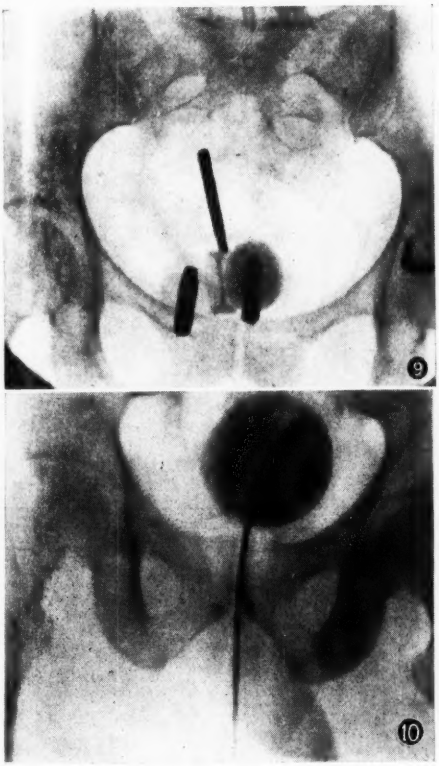


Fig. 9. Radio-active cobalt tubes in the uterus and fornices for treatment of a carcinoma of the cervix on the Manchester scheme.

Fig. 10. Cones' catheter with radio-active beads for the treatment of carcinoma of the bladder. The circle around the bead is due to coloured sodium iodide in the balloon, so that if a leak occurs it will be detected as soon as possible.

B. FOR THERAPEUTIC PURPOSES

Within the limitations I have already mentioned, i.e. with the exception of the very short-life isotopes and the massive quantities in the form of cobalt bombs, we use the same isotopes which have been used or are being used abroad. The radio-isotope techniques are:

1. *As External Applicators*: *Cobalt*^{60}. This we use in the form of rods of 5 mc. strength, larger rods of 50 mc., and beads of 40–50 mc. A number of these can be made up in ovoids for gynaecological work according to the Manchester scheme[28] (Fig. 9). We use them as beads of 50 and 40 mc. strength for special applicators which we have had made for the treatment of naso-pharyngeal growths or for bladder carcinoma (Fig. 10). By putting the tubes or beads in various holders, the required applicators can be made for intra-cavitary work, e.g. the antrum, the frontal sinuses, the oesophagus (Figs. 11–14).

The bladder applicator (Fig. 10) was designed by Cones and Gregory.[29] It consists of a central cobalt source surrounded by a balloon which is inflated and into which coloured sodium iodide is introduced. The balloon is distended to fit the bladder and, by radiography, it is possible to work out the dose at the periphery of the bladder. This method has proved very useful in cases of multiple growths of the bladder.

The cobalt can, of course, be made into plaques as surface applicators.

Although we have P^{32}, I do not think it is practicable to use P^{32} as a surface applicator of the blotting paper type, because there are not so many cases of keratoses and very superficial rodent ulcers (for which Low-Beer designed these applicators); also, the cost of radio-phosphorus is relatively high.

Phosphorus is an expensive isotope to import for use here. With a half-life of 14 days, it is not feasible. Moreover, the lesions for which P^{32} can be used as a surface applicator can be treated much more readily with low voltage X-rays from the contact type X-ray machine.

Sr^{90} applicators for the eyes consist of a number of shells designed for different purposes:[30]

i. For irradiating the cornea in front of the globe only.
ii. For irradiating the whole conjunctival sac.
iii. A ring for irradiating corneal grafts; and
iv. A spot about 0.5 cm. in diameter for irradiating isolated lesions and corneal blood vessels.

In our experience the Perspex becomes cracked as a result of the radiation. It is

understood, however, that new types of applicators are being designed using different material.* We have found Sr^{90} applicators a very useful and simple means of applying beta radiation to the eye.

*We have now received these new strontium eye applicators.

Interstitial. Cobalt needles adequately covered with steel tubes (cobalt itself is poisonous to the tissues) may be used for interstitial purposes. They have some advantage in that they can be made in various shapes and sizes to conform to various curved contours, e.g. the bladder.[31] Cobalt beads have also been

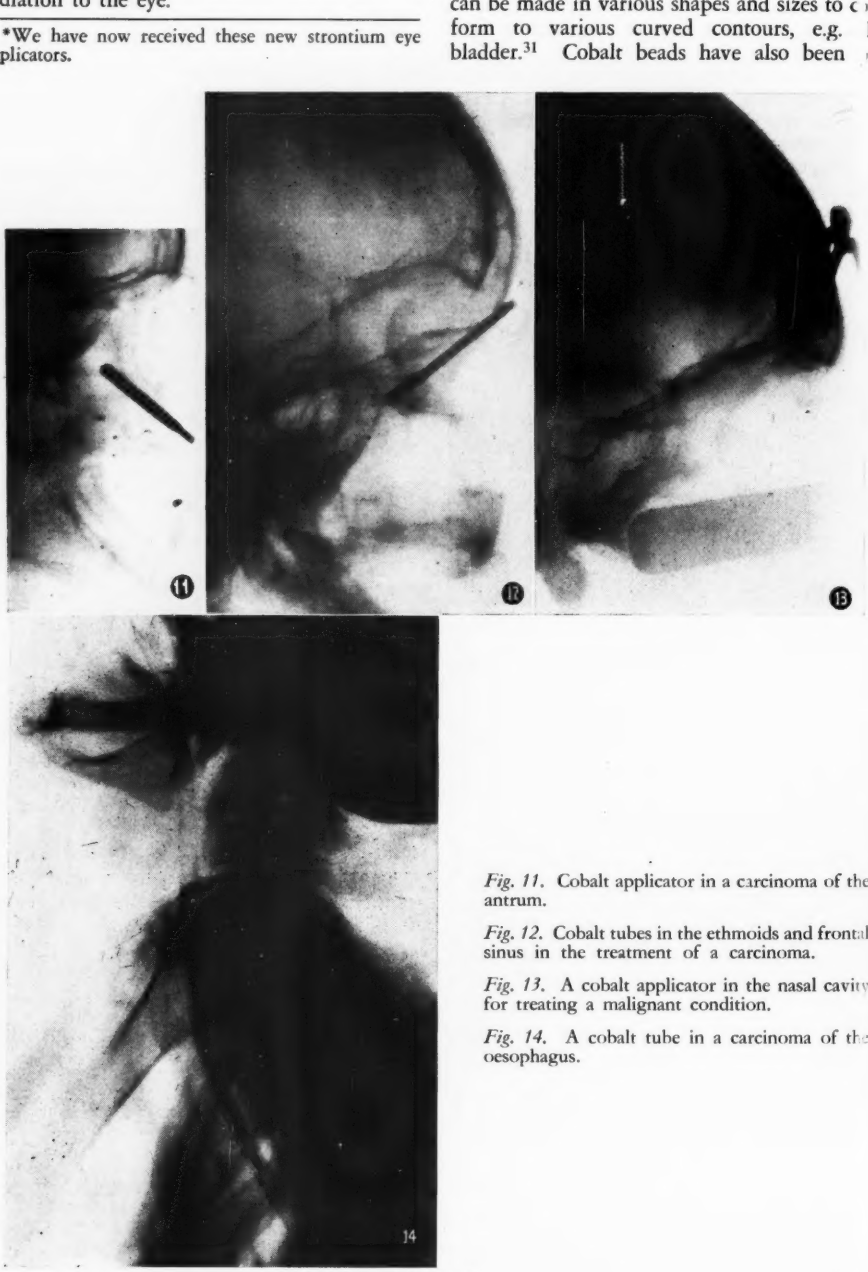


Fig. 11. Cobalt applicator in a carcinoma of the antrum.

Fig. 12. Cobalt tubes in the ethmoids and frontal sinus in the treatment of a carcinoma.

Fig. 13. A cobalt applicator in the nasal cavity for treating a malignant condition.

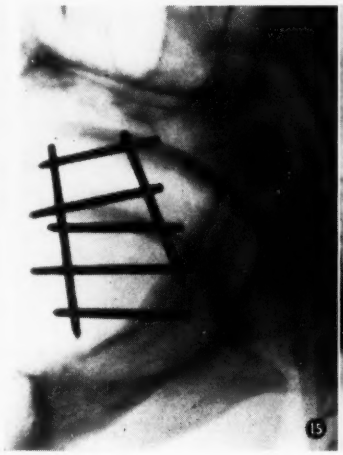
Fig. 14. A cobalt tube in a carcinoma of the oesophagus.

into nylon tubes and drawn through the tissues as an implant.

I have no knowledge of either cobalt needles or cobalt in nylon tubes having been used in South Africa. We prefer to use radium needles, as we have a sufficient number of them. For those who have not got radium needles and are equipping or intend equipping new departments, there will be some advantage in obtaining cobalt needles because they are much cheaper than radium needles.

Cobalt needles are used in exactly the same way as radium needles. Figs. 15–19 show implantation of the tongue, the cheek, the breast and the bladder. These can be done either with cobalt or radium needles, the techniques being identical.

Radio-Active Gold Seeds. Hitherto we have preferred radon seeds, simply because of the longer half-life which makes it safer to plan one's work here. For certain purposes we are switching over to gold seeds or yttrium, e.g. implantation of the pituitary for secondary deposits from the breast or the prostate. We have done a number of these cases now.[9] The following figures illustrate the method (Figs.



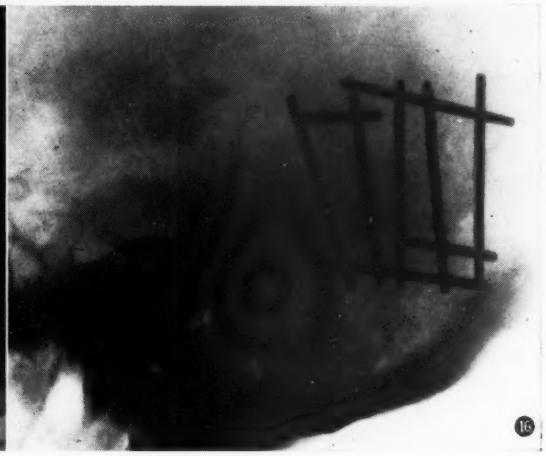


Fig. 15. A radium implant in a carcinoma of the cheek. Radio-active cobalt tubes can be used in an identical manner.

Fig. 16. Radium implant into a large epithelioma of the scalp. Radio-active cobalt needles can be used in exactly the same way.

Fig. 17. Volume implant into an extensive carcinoma of the tongue and floor of the mouth.

Fig. 18. A radium implant into an inoperable growth of the breast. Radio-active cobalt tubes could be used in an identical manner.

Fig. 19. Lateral view of a radium or cobalt implant into a carcinoma of the bladder.

Fig. 20. Apparatus and technique for implanting radon, radio-active gold or yttrium into the pituitary. We are indebted to Dr. Peter Kerley for this photograph.

Fig. 21. To show the trocar in the correct position to penetrate the floor of the pituitary fossa.

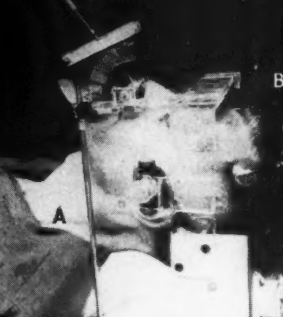


Fig. 22. The second of 2 seeds has just been introduced into the pituitary gland.

20–22). The technique is identical, whether one uses radio-active gold seeds or radon, but the quantities are, of course, different. We have switched over to radio-active yttrium instead of radon for this purpose because of the visual disturbances which have been reported and which have been attributed to the gamma component of the radon. Radio-active gold has consequently been used both on the Continent and at the Royal Marsden Hospital. Yttrium takes longer to reach here than radon, which we obtain within 7–10 days of placing the order; whereas yttrium takes about 3 weeks. This interval will no doubt be reduced when the demand for yttrium overseas becomes greater.†

Radio-active gold seeds are used for interstitial implants instead of radon for bladder lesions, skin lesions, in the mouth, in the tongue and mediastinum, as Figs. 23–27 indicate. In most cases, in the final result there is not a great deal of difference between radio-active gold seeds and radon. In cases such as haemangioma in infants (Fig. 28) it would be an advantage to use gold rather than radon to avoid any risk of interfering with the development of muscles and underlying bones by the penetrating gamma rays. In Fig. 28 long radon seeds with an active length of 1 mc. per cm. were used, according to a technique we have seen at the Westminster Hospital (Sir Stanford Cade); but in similar cases in future we intend using radio-active gold. The equivalent implants are: 1 millicurie of radon = 5 millicuries gold when allowing for the difference in K factors and half-life values.[32] The difference in the use of radon and radio-active gold is dictated here by convenience for South African conditions.

Tantalum[182] wire is sheathed in platinum and has been used for interstitial work, e.g. carcinoma of the bladder, and has the advantage that it can be more easily withdrawn than radium needles after the desired dose has been

†Recently we have obtained yttrium supplies from Harwell within one week.

delivered. Tantalum has a half-life of 111 days and a K factor of 6.13 r/h/mc. Consequently 1 mg. of radium filtered with 0.5 mm. platinum is equivalent to 1.35 mc. tantalum[182]. It has also been used for applicators in ophthalmology.[33]

Direct Infiltration. Gold, silver, colloidal chromic phosphate and P^{32} have been used for direct infiltration (suggested by Hahn and Sheppard).[5] Of these we have only used Au^{198}. It has been used for carcinoma of the prostate[34] and the first 20 cases treated reacted without any accidents. The subsequent 20, because of leakage from the prostate on to the rectum, gave rise to a number of rectal ulcers. These were so severe that in some instances a colostomy had to be performed. We have used the technique for a mass infiltrating the pouch of Douglas, which did not respond to the amount of 250 K.V. X-rays which we could get into it. It was consequently infiltrated with gold. The mass disappeared but unfortunately a rectal ulcer, an extremely painful condition, developed. I do not know of any other cases in which it has been used in South Africa. We have also infiltrated Au^{198} directly into secondary deposits in the lung (from a seminoma) through the chest wall under screen control, but as the patient was in a hopeless condition, it was not possible to say what the effect was.

Intra-Cavitary. The use of $cobalt^{60}$ for carcinoma of the bladder in suitable cases as a central source at the end of a catheter surrounded by a balloon filled with coloured sodium iodide has already been described. We also use cobalt tubes in gynaecological work instead of radium on the Manchester system.[28]

Sodium[24] and bromine[82] are used for bladder work at the Royal Marsden Hospital, London,[35] but cannot be used here.

Following a visit to Dr. Ellis at Oxford in 1953, we started using colloidal gold for bladder work in such conditions as papillomata.

We use a good deal of gold for intraperitoneal and intrapleural work in an attempt to stop or diminish the formation of malignant effusions.[35] We have had some very good results in both the intrapleural and intraperitoneal cases. We have treated some 90 cases.

In collaboration with Mr. A. Mendelow we have injected gold into 2 cases of Rathke's pouch cysts with very good results in both cases (Fig. 29).

Leksell and Linden[36] have used P^{32} for injection into a cystic naso-pharyngioma.

Intravenous and Intra-Oral. The first isotope used for intravenous and intra-duodenal administration was radio-active sodium.[2] P^{32}, however, has played a much greater role in this type of treatment, because of the use of P^{32} for polycythaemia and the leukaemias. P^{32} can be given either by mouth or intravenously.[37]

There is some advantage in giving it intravenously in that less is lost. Intravenous P^{32} is mainly excreted through the urine and, when given by mouth, through the faeces. We used more P^{32} originally than we do now. Formerly, we used it in the treatment of myeloid and lymphatic leukaemia as well as polycythaemia. There is no real advantage in using it in South Africa, at any rate, because of the

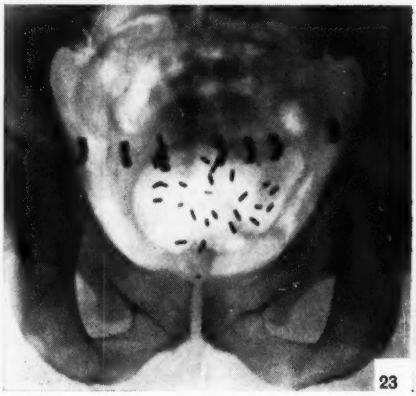


Fig. 23. Radon implant into a bladder. Radio-active gold seeds could be used in the same way.
Fig. 24. Implant of radon or radio-active gold into the tongue and the floor of the mouth.

expense. For the leukaemias chemotherapy gives good results and the mainstay in these conditions is X-ray therapy in any case. The latter has the advantage that it can be controlled much more easily than can P^{32}. Once P^{32} is injected or taken intra-orally, its effect cannot be regulated. In South Africa at present one cannot use it in small repeated doses, as Low-Beer suggested, because of the expense. We have to use it in large doses of 5–8 mc. Sodium for intravenous work has not been used because of its low half-life. We use P^{32} for all cases of polycythaemia vera.[37]

The isotope which is used most in South Africa is radio-active iodine. This we use almost entirely by mouth in the treatment of thyrotoxicosis and carcinoma of the thyroid, both in diagnosis and therapy, and in the treatment of angina.[38] Iodine as a diagnostic procedure for thyrotoxicosis and in some instances carcinoma of the thyroid, is unequalled.

As a therapeutic measure in certain types of thyrotoxicosis, I^{131} is unparalleled for its value. The controversy whether other methods of treatment (surgery and drugs) compare favourably with radio-active iodine, still goes on; but

Fig. 25. A radon implant into an epithelioma over the nose which has been treated previously and has broken down.

Fig. 26. A radon implant into an epithelioma of the tonsil.

Fig. 27. A radon implant into the carina and carcinoma of the bronchus.

there can be no doubt that for the soft, diffusely enlarged thyroid associated with thyrotoxicosis, it is the treatment of choice. Although surgery in expert hands gives excellent results and has almost no mortality,[39] it is nevertheless an operation, whereas radio-active iodine treatment is merely a drink. For the nodular thyroid, radio-active iodine is not quite so valuable, although the nodular thyroid does respond in the end to much larger doses;[40] but there is the risk, under certain conditions, of overlooking an inactive nodule which may be malignant. Thyrotoxicosis is seldom associated with carcinoma of the thyroid, but this does occur at times. We have had several such cases.

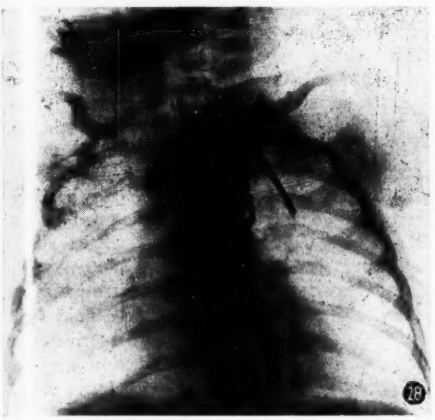


Fig. 28. Long radon seeds in a cavernous haemangioma.

Fig. 29. A radio-active gold injection into a Rathke's pouch cyst outlined by the specks of calcification. This patient did very well after this radio-active gold injection. (In collaboration with Mr. H. Mendelow.)

There is no doubt that I^{131} is of great value in some cases. Only 16–20% of thyroid carcinomas will take up the radio-active iodine. The papillary adenocarcinoma of the thyroid is a frequent type of carcinoma, particularly in younger age groups, and will not take up any quantity of radio-active iodine; but the alveolar or colloid type does take up I^{131}. The undifferentiated type will not, but thyroid tumours are seldom of uniform cellular type. They may be mixed and frequently are of the mixed cell type tumour. Nielsen[42] has advised that all cases of carcinoma of the thyroid should be given radio-active iodine so that any outlying secondaries, which may not even be demonstrable on X-ray, because they are too small, would be radiated to some extent.

The results, when the secondary deposits do take up radio-active iodine, may be very dramatic. Fig. 5 is of a patient with a big defect in the occipital bone who is perfectly fit after radio-active iodine treatment. He had some hundreds of millicuries of radio-active iodine over a period of years, and although the bone has not regenerated (it seldom does in carcinoma of the thyroid) the result has been remarkable. Similarly, Fig. 6 shows a case of secondary deposits in the pelvis and the lumbar and dorsal spine. The result has also been outstanding. This unfortunate patient had a carcinoma of the thyroid which was overlooked. She had secondary deposits in the spine and pelvis which were overlooked. Ultimately the diagnosis was made and when she was sent for treatment to Johannesburg, we could not give her X-ray treatment because of the agony it caused when she was moved. She could not walk, she could not turn over in bed, she seemed to be in a hopelessly painful state, crying with agony most of the time. She was given radio-active iodine treatment only, after tracer tests which showed that the iodine was taken up in various parts of the pelvis and the spine. The result has been dramatic. It is true that it took a long time and large quantities of radio-active iodine running into some hundreds of millicuries, but in the end the patient could walk quite comfortably.

In the other malignant conditions the isotopes are only used as a means of delivering as conveniently as possible the beta and gamma radiations. As we have already mentioned, the cobalt and the caesium bombs which we have not yet got but will get, simply take the place of radium or high voltage radiation. They are used because of the cheapness of the isotope and thus there is the possibility of using large quantities in the region of 1,000–3,000 curies compared with the largest radium bomb in England (10 grammes) or the largest in Belgium (50 grammes) used by Professor Maisin. A 1,000 curie radium bomb would cost about £8 million. The 1,000 curie cobalt bomb with the apparatus only costs about £15,000.

Intravenous gold has been used for secondary deposits in lungs.[41] In several cases we have used it intravenously and some of the secondary deposits from an Ewing sarcoma in the lungs have cleared up that way. The difficulty with intravenous gold is that the particles are so small that, when used for secondary deposits in the lungs, they pass through the lung and do not give sufficient radiation. Muller has suggested using a larger colloid particle and has this made up in Switzerland and sent to England for irradiation or activation and sent back to him. This is rather too complicated a procedure for South Africa and we have used it as the colloid which is usually supplied.

So, of all the hundreds of isotopes, there are only a very few which are of any use either for specific treatment or for treatment as an external radiator.

The great hope and aim of those using or experimenting with isotopes, is to make or find an isotope which will be absorbed by any one particular tissue in the same manner as radio-active iodine. Unfortunately, this has not yet materialized. It would be a great advance, for instance, if one could synthesize radio-active carbon into some compound which would be absorbed by the malignant melanomata. Although as long ago as 1947 Lawrence expressed hopes in that direction, it has not yet proved successful.

It is hoped that this review gives some idea of the extent to which we use isotopes in South Africa. This will naturally increase. We hope you have also gathered how useful it might be in less accessible places than Pretoria and Johannesburg. One learns with amazement that there is no radiotherapy between Southern Rhodesia and (according to the press) Italy. I think this must be a mistake, as there must be some radiotherapy in Egypt; but the vast areas in Central Africa, British East Africa, Tanganyika, Uganda and Nyasaland and I assume, the Belgian and French Congos and Portuguese territories, have no radiotherapy facilities. One can understand the difficulties of installing heavy, large and expensive X-ray machines which are difficult to maintain because of the necessity for skilled mechanics, and the difficulties in transport of spare parts and so on; but in the isotopes one can meet a great deal of the demand for radiotherapy particularly if the territories concerned are prepared to put in radio-active cobalt bombs and later on, after 1960 when it becomes available, caesium bombs; but there is no need to wait so long to make a start. They can all get radio-active cobalt needles, radio-active phosphorus for the treatment of the leukaemias and other blood dyscrasias, radio-active gold (whether in liquid or solid form), radio-active cobalt for needling, intracavitary and plaque purposes. There is no difficulty, as far as I can see, in obtaining any of these which are so very useful in the immediate treatment of accessible cancer. We do not know the exact incidence of the various diseases we have mentioned amongst the various populations in Africa south of the Sahara. Carcinoma of the cervix, we are told, exists in Central Africa to a great extent. Radio-active cobalt applicators would be very useful for many of these cases.

We have indicated the use of radio-active cobalt tubes for the treatment of carcinoma of the antrum and of the ethmoidal regions and elsewhere. For carcinoma of the tongue, cobalt in the form of needles could be used, so that a large percentage of the type of cancer which is curable, i.e. accessible cancer, could be treated at once without waiting for expensive X-ray machines or large radio-active bombs.

There can be no reasonable excuse for delaying the introduction of this form of radiotherapy, provided the trained personnel is available.

OPSOMMING

1. Die geskiedenis van die invoering in 1948 van radio-aktiewe isotope vir mediese diagnose en terapie, en die invoering van radon vir terapeutiese doeleinde in 1950 word beskryf.

Radio-isotope is in Suid-Afrika in gebruik geneem kort nadat president Truman in 1947 op die Kankerkongres in die Verenigde State aangekondig het dat

die uitvoer van radio-aktiewe isotope in die toekoms toegelaat sou word. Gelyktydig met die Europese lande kon Suid-Afrika dus radio-aktiewe isotope vir mediese doeleindes in diens neem.

Die invoering van radon moes wag tot 1950 weens die moeilikhede wat deur vervoer opgelewer is. Eers nadat 'n vinnige lugdiens beskikbaar gestel is, kon dit in gebruik geneem word.

2. Die regulasies in verband met die gebruik van radio-isotope, soos neergelê deur die Komitee vir Wetenskaplike en Nywerheidsnavorsing en die Atoomkragraad, word bespreek.

3. Die isotope wat gebruik word vir goedaardige en kwaadaardige toestande word in Tabelle 1–3 uiteengesit.

4. Die waarde word aangedui van die verskillende isotope vir diagnostiese doeleindes, soos radio-aktiewe jodium vir die diagnose van skildkliervergiftiging, en radio-aktiewe fosfor vir die demonstrasie van die omvang van breingewasse en die beste posisie vir die verkryging van biopse-materiaal.

5. Die syfers wat verwag kan word in radio-aktiewe jodiumopneming by normale en hiper-skildklier gevalle word in die grafieke aangetoon.

6. Die waarde van verskillende radio-aktiewe jodiumtoetse word bespreek.

7. Aan terapeutiese kant word die waarde van radio-aktiewe jodium by die behandeling van sekondêre neerslae uit die skildklier in gevalle wat radio-aktiewe jodium opneem, gedemonstreer by sommige pasiënte met sekondêre neerslae in die skedel, die bekken en die ruggraat.

8. Die gebruik van en die tegniek wat toegepas word met die verskillende isotope, soos kobalt in die vorm van naalde vir interstisiële werk of vir telecurie-doeleindes word aangedui.

9. Insgelyks word die gebruik van radio-aktiewe fosfor, radio-aktiewe stronsium, radio-aktiewe goud in vloeibare vorm en goudsaad bespreek.

10. Aangesien radio-terapie op die oomblik nie in Sentraal-Afrika beskikbaar is nie, word daar aan die hand gedoen dat hierdie soort behandeling met baie min moeite en sonder vertraging in geskikte gevalle van stapel gestuur kan word deur die gebruik van radio-aktiewe isotope en radium en radon, tot tyd en wyl ten volle toegeruste radio-terapie-afdelings tot stand gebring kan word.

We wish to thank Prof. S. M. Naude and the isotope staff of the C.S.I.R. for their invaluable assistance since the isotope work started in 1948. They have at all times obtained whatever isotopes we have required and they have always been only too ready to help with technical advice.

We also wish to acknowledge our indebtedness to Dr. M. M. Suzman, Dr. F. P. Reid and Dr. R. Morris for their cooperation on the clinical side of the investigations and for their critical interest in this field of work, particularly in connexion with radio-active iodine.

It is a pleasure to acknowledge also the interest shown by Mr. D. Adler and Mr. D. Fuller in the use of radon and of radio-active cobalt and gold in the thoracic field.

Other medical and surgical colleagues, too numerous to mention individually, have materially contributed to the development of the radio-active isotope programme since its inception in South Africa..

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